

Amendments to the Claims

Please amend Claims 1-3, 10-11, 25-27, 29 and 51.

Please cancel Claim 5, 30 and 54-56.

Please add new Claims 58-63.

The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

1. (Currently Amended) A method of characterizing a ~~multi-determinant~~ metabolic phenotype of an individual, ~~wherein a plurality of phenotypic determinants are identified as corresponding to respective metabolic characteristics, said method comprising:~~
 - a. administering to ~~an~~ said individual a probe substrate specific to a metabolic pathway ~~of each of said plurality of phenotypic determinants;~~
 - b. detecting metabolites of said probe substrate ~~metabolic pathways~~ in a biological sample from said individual in response to said probe substrate, wherein said biological sample is not a breath sample; and
 - c. characterizing ~~respective phenotypic determinants of said multi-determinant~~ metabolic phenotype of said individual based on detected metabolites to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual.
2. (Currently Amended) The method of claim 1 which further comprises a step i) after step b): i) quantifying a ratio of respective detected metabolites for ~~each of said metabolic pathways~~ probe substrate in said biological sample.
3. (Currently Amended) The method of claim 2, wherein said ratio is selected from the group consisting of concentration ratio, molar ratio, chiral ratio, ~~ratio of area under the curve~~ and ~~signal~~ peak height ratio.

4. (Original) The method of claim 1 wherein said probe substrate is at least one probe substrate known to be metabolized by said metabolic pathway.
5. (Canceled)
6. (Original) The method of claim 1, wherein said step b) and/or c) is effected using an affinity complexation agent specific to each of said metabolites.
7. (Original) The method of claim 6, wherein said affinity complexation agent is an antibody.
8. (Original) The method of claim 7, wherein said antibody is a monoclonal antibody.
9. (Original) The method of claim 7, wherein said antibody is a polyclonal antibody.
10. (Currently Amended) The method of claim 6, wherein said affinity complexation agent is a ~~molecular~~ molecularly imprinted polymer.
11. (Currently Amended) The method of claim 6, wherein said affinity complexation agent is an ~~aptmer~~ aptamer.
12. (Original) The method of claim 6, wherein said affinity complexation agent is a receptor.
13. (Original) The method of claim 6, wherein said affinity complexation agent is an anticalin.
14. (Original) The method of claim 6 further comprising a ligand binding assay.

15. (Original) The method of claim 14 wherein said ligand binding assay is selected from the group consisting of immunoassay, enzyme-linked immunosorbent assay (ELISA), microarray formatted immunoassay and microarray formatted ELISA.
16. (Original) The method of claim 14, wherein said ligand binding assay is a rapid immunoassay (Dipstick assay).
17. (Original) The method of claim 16, wherein said rapid immunoassay is based on Rapid Analyte Measurement Platform (RAMP) technology.
18. (Original) The method of claim 16, wherein said rapid immunoassay is based on light-emitting immunoassay technology.
19. (Original) The method of claim 14 wherein said ligand binding assay is performed with a biosensor.
20. (Original) The method of claim 19 wherein said biosensor is an immunosensor.
21. (Original) The method of claim 19 wherein the means of detection of said biosensor is an electrochemical sensor.
22. (Original) The method of claim 19, wherein the means of detection of said biosensor is an optical sensor.
23. (Original) The method of claim 19, wherein the means of detection of said biosensor is a microgravimetric sensor.
24. (Original) The method of claim 23, wherein said microgravimetric sensor is a quartz crystal microbalance (QCM).

25. (Currently Amended) The method of claim 1, wherein step b) is effected using a ~~qualitative~~ quantitative detection instrument.
26. (Currently Amended) The method according to claim 1, wherein ~~each of said plurality of phenotypic determinants of said multi-determinant~~ metabolic phenotype is characterized in step c) based on an enzyme-specific determinant detected metabolites.
27. (Currently Amended) The method according to claim 26 wherein said ~~multi-determinant~~ metabolic phenotype is comprised of at least one metabolite determinant indicative of an individual's metabolic capacity for at least one drug metabolizing enzyme.
28. (Original) The method of claim 27 wherein the said at least one drug metabolizing enzyme is selected from the group consisting of CYP1A2, N-acetyltransferase-1 (NAT-1), N-acetyltransferase-2 (NAT-2), CYP2D6, CYP2A6, CYP2E1, CYP3A4, CYP2C9, CYP2C19, UGTs, GSTs, and SUT.
29. (Currently Amended) The method of claim 2, wherein step a) is effected using a ~~plurality of at least two~~ probe substrates and wherein each probe substrate is specific to at least one metabolic pathway of interest.
30. (Canceled)
31. (Withdrawn) A method of using a multi-determinant metabolic phenotype to select a drug treatment regimen for an individual, said method comprising, comparing a metabolic profile of a candidate drug with said multi-determinant metabolic phenotype of said individual, and selecting said candidate drug for use in said treatment regimen for said individual when said multi-determinant metabolic phenotypic is indicative of a phenotype having metabolic efficiency for said candidate drug.

32. (Withdrawn) A method of using a multi-determinant metabolic phenotype to select a drug treatment regimen for an individual, said method comprising comparing a metabolic profile of a candidate drug with said multi-determinant metabolic phenotype of said individual, wherein said multi-determinant metabolic phenotype is characterized according to the method of Claim 1, and selecting said candidate drug for use in said treatment regimen for said individual when said multi-determinant metabolic phenotypic is indicative of a phenotype having metabolic efficiency for said candidate drug.
33. (Withdrawn) A method of using a multi-determinant metabolic phenotype to individualize a selected drug treatment regimen for an individual, wherein said multi-determinant metabolic phenotype of said individual is characterized; a safe and therapeutically effective dose of said drug treatment is determined for said individual based on said multi-determinant phenotype; and said dose for use in said selected treatment regimen for said individual is selected based thereon.
34. (Withdrawn) A method of using a multi-determinant metabolic phenotype to individualize a selected drug treatment regimen for an individual, wherein said multi-determinant metabolic phenotype of said individual is characterized according to the method of Claim 1; a safe and therapeutically effective dose of said drug treatment is determined for said individual based on said multi-determinant phenotype; and said dose for use in said selected treatment regimen for said individual is selected based thereon.
35. (Withdrawn) The method of claim 33, wherein said drug treatment is selected from a class or genus of compounds with similar metabolic profiles.
36. (Withdrawn) The method of claim 35 wherein said drug treatment regimen is selected according to the method comprising:
 - a. administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;

- b. detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and
 - c. characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.
37. (Withdrawn) A method of using a multi-determinant metabolic phenotype to individualize a selected drug treatment regimen for an individual, wherein said drug treatment is selected from a class or genus of compounds with similar metabolic profiles; and wherein said multi-determinant metabolic phenotype of said individual is characterized according to the method of Claim 1; a safe and therapeutically effective dose of said drug treatment is determined for said individual based on said multi-determinant phenotype; and said dose for use in said selected treatment regimen for said individual is selected based thereon.
38. (Withdrawn) A method of treating an individual having a medical condition with a safe and therapeutically effective dose of a drug treatment known for use with said condition, said method comprising:
- a. characterizing a multi-determinant metabolic phenotype of said individual; and
 - b. administering a safe and therapeutically effective dose of at least one compound known for treating said condition, wherein said at least one compound known for treating said condition has a metabolic profile corresponding to said individual's metabolic phenotype for said at least one compound as represented by said multi-determinant metabolic phenotype.
39. (Withdrawn) A method of treating an individual having a medical condition with a safe and therapeutically effective dose of a drug treatment known for use with said condition, said method comprising:
- a. characterizing a multi-determinant metabolic phenotype of said individual according to the method of Claim 1; and

- b. administering a safe and therapeutically effective dose of at least one compound known for treating said condition, wherein said at least one compound known for treating said condition has a metabolic profile corresponding to said individual's metabolic phenotype for said at least one compound as represented by said multi-determinant metabolic phenotype.
40. (Withdrawn) A method of selecting a treatment for an individual corresponding to said individual's multi-determinant metabolic phenotype, said method comprising:
- a. characterizing a multi-determinant metabolic phenotype of said individual;
 - b. identifying a treatment from a group of candidate treatments that corresponds to said individual's multi-determinant metabolic phenotype; and
 - c. selecting said treatment.
41. (Withdrawn) A method of selecting a treatment for an individual corresponding to said individual's multi-determinant metabolic phenotype, said method comprising:
- a. characterizing a multi-determinant metabolic phenotype of said individual according to the method of Claim 1;
 - b. identifying a treatment from a group of candidate treatments that corresponds to said individual's multi-determinant metabolic phenotype; and
 - c. selecting said treatment.
42. (Withdrawn) A method of screening a plurality of individuals for participation in a drug treatment trial assessing the therapeutic effect of a candidate drug treatment, said method comprising:
- a. characterizing a multi-determinant metabolic phenotype of each of said plurality of individuals;
 - b. identifying those individuals having a metabolic phenotype characterized as effective for metabolizing said candidate drug treatment.

43. (Withdrawn) A method of screening a plurality of individuals for participation in a drug treatment trial assessing the therapeutic effect of a candidate drug treatment, said method comprising:
- a. characterizing a multi-determinant metabolic phenotype of each of said plurality of individuals according to the method of Claim 1;
 - b. identifying those individuals having a metabolic phenotype characterized as effective for metabolizing said candidate drug treatment.
44. (Withdrawn) An assay system for detecting the presence of multiple determinant-specific metabolites in a biological sample obtained from an individual treated with at least one probe substrate specific for metabolic pathways of said metabolites; said system comprising:
- a. means for receiving said biological sample, including a plurality of affinity complexation agents contained therein;
 - b. means for detecting presence of said metabolites bound to said affinity complexation agents; and
 - c. means for quantifying ratios of said metabolites to provide corresponding phenotypic determinants;
- wherein said phenotypic determinants provide a multi-determinant metabolic phenotype of said individual.
45. (Withdrawn) The assay system of claim 44, wherein said probe substrate is other than an inducer or inhibitor of said metabolic pathway.
46. (Withdrawn) An assay system for detecting the presence of multiple determinant-specific metabolites in a biological sample obtained from an individual treated with at least one probe substrate specific for metabolic pathways of said metabolites, said system comprising:
- a. means for receiving said biological sample, including a plurality of affinity complexation agents contained therein;

- b. means for detecting presence of said metabolites bound to said affinity complexation agents; and
 - c. means for quantifying ratios of said metabolites to provide corresponding phenotypic determinants;
- wherein said phenotypic determinants provide a multi-determinant metabolic phenotype of said individual and said steps b) and/or c) are effected according to the method of claim 6.
47. (Withdrawn) The assay system of claim 44 wherein said means for receiving said biological sample is a multi-well microplate including said plurality of affinity complexation agents in each well.
48. (Withdrawn) The assay system of claim 47 wherein said plurality of affinity complexation agents are bound to each well in an array-based format.
49. (Withdrawn) The assay system of claim 48 wherein said means for detecting said presence of said metabolites bound to said binding agents is a charge-coupled device (CCD) imager.
50. (Withdrawn) The assay system of claim 44 wherein said means for said quantifying ratios of said metabolites is a densitometer.
51. (Currently Amended) A method of using a ~~multi-determinant~~ metabolic phenotype of claim 1 for determining a combination drug therapy wherein an individual's phenotype is indicative of a fast metabolizer, and a corresponding inhibitor of a drug is selected for combined treatment with a the drug to improve the therapeutic effect of the drug thereof in said individual.
52. (Withdrawn) A method of diagnosing a disease or condition associated with altered function in a drug metabolizing enzyme(s) by characterizing an

individual's multi-determinant metabolic phenotype.

53. (Withdrawn) A method of diagnosing a disease or condition associated with altered function in a drug metabolizing enzyme or enzymes by determining an individual's multi-determinant metabolic phenotype wherein said multi-determinant metabolic phenotype is characterized according to the method of Claim 1.

54-56. (Canceled)

57. (Withdrawn) An assay system for characterizing a multi-determinant metabolic phenotype, wherein a plurality of phenotypic determinants are identified as corresponding to respective metabolic characteristics, said assay system comprising:
- a. means for administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;
 - b. means for detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and
 - c. means for characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.
58. (New) A method of characterizing a metabolic phenotype of an individual, comprising:
- a. administering to the individual at least two probe substrates, wherein each probe substrate is specific to at least one metabolic pathway of interest;
 - b. detecting metabolites of each of the probe substrates in a biological sample from the individual in response to the probe substrate, wherein the biological sample is not a breath sample; and
 - c. characterizing the metabolic phenotype of the individual based on detected metabolites to individualize a selected safe and therapeutically effective drug treatment dosing regimen for the individual.

59. (New) A method of determining an individual's drug metabolizing ability, comprising:
- a. characterizing a metabolic phenotype of the individual according to the method of Claim 1, wherein the individual is administered a probe substrate specific to a metabolic pathway of the compound prior to exposure of the individual to the compound, thereby determining a pre-compound exposure phenotype;
 - b. exposing the individual to the compound;
 - c. characterizing a metabolic phenotype of the individual according to the method of Claim 1, wherein the individual is administered a probe substrate specific to a metabolic pathway of the compound after exposure of the individual to the compound, thereby determining a post-compound exposure phenotype; and
 - d. comparing the phenotype determined in step a) with the phenotype determined in step c), whereby a difference between the phenotypes indicates the individual's drug metabolizing ability.
60. (New) The method of claim 59, wherein the individual is a mammal.
61. (New) The method of claim 60, wherein the mammal is a human.
62. (New) A method of individualizing a selected safe and therapeutically effective drug treatment dosing regimen for an individual, comprising:
- a. administering to the individual a probe substrate specific to a metabolic pathway, wherein the probe substrate is a substrate of the metabolic pathway;
 - b. detecting metabolites of the probe substrate in a biological sample from the individual in response to the probe substrate using a detection device, wherein the biological sample is not a breath sample, resulting in detected metabolites;
 - c. quantifying a ratio of the detected metabolites in step b), wherein the ratio is selected from the group consisting of concentration ratio, molar ratio, chiral ratio and signal peak height ratio; and

- d. characterizing the metabolic phenotype of the individual based on detected metabolites to individualize a selected safe and therapeutically effective drug treatment dosing regimen for the individual, using a detection device.
63. (New) A method of characterizing a metabolic phenotype of an individual, comprising:
- a. administering to the individual a probe substrate specific to a metabolic pathway;
 - b. detecting metabolites of the probe substrate in a biological sample from the individual in response to the probe substrate, wherein the biological sample is selected from the group consisting of tissue, cerebrospinal fluid, plasma, serum, saliva, blood, nasal mucosa, urine, synovial fluid and microcapillary microdialysis; and
 - c. characterizing the metabolic phenotype of the individual based on detected metabolites to individualize a selected safe and therapeutically effective drug treatment dosing regimen for the individual.